

Applicant : Or et al.
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In the claims:

Please amend the claims as follows:

1. (Currently Amended) A cyclosporin analog of formula (I), or a its pro-drug or a pharmaceutically acceptable salt thereof:

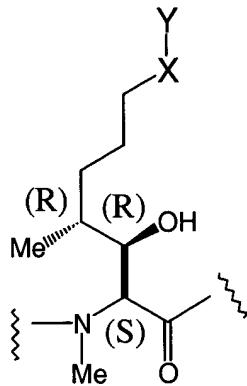
A---B---Sar-MeLeu-Val-MeLeu-Ala---U---MeLeu-MeLeu-MeVal

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(I)

wherein,

(a) A is of the formula:



wherein

- X is absent, -C1-C6 alkyl-, or -C3-C6 cycloalkyl-;
- Y is selected from the group consisting of:
 - i. -C(O)-O-R1 where R1 is hydrogen, C1-C6 alkyl optionally substituted with halogen, heterocyclics, aryl, C1-C6 alkoxy or C1-C6 alkylthio, halogen substituted C1-C6 alkoxy, or halogen substituted C1-C6 alkylthio;
 - ii. -C(O)-S-R1 where R1 is hydrogen, C1-C6 alkyl optionally substituted with halogen, heterocyclics, aryl, C1-C6 alkoxy

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or C1-C6 alkylthio, halogen substituted C1-C6 alkoxy, or
 halogen substituted C1-C6 alkylthio;

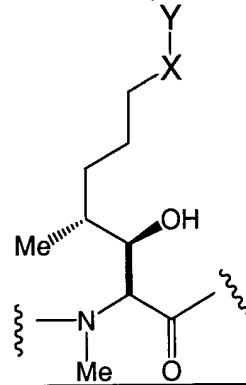
- iii. -C(O)-OCH₂-OC(O)R₂ where R₂ is C1-C6 alkyl, optionally substituted with halogen, C1-C6 alkoxy, C1-C6 alkylthio, heterocyclics or aryl;
- iv. -C(S)-O-R₁ where R₁ is hydrogen, C1-C6 alkyl optionally substituted with halogen, heterocyclics, aryl, C1-C6 alkoxy or C1-C6 alkylthio, halogen substituted C1-C6 alkoxy, or halogen substituted C1-C6 alkylthio; and
- v. C(S)-S-R₁ where R₁ is hydrogen, C1-C6 alkyl optionally substituted with halogen, heterocyclics, aryl, C1-C6 alkoxy or C1-C6 alkylthio, halogen substituted C1-C6 alkoxy, or halogen substituted C1-C6 alkylthio.

- (b) B is -αAbu-, -Val-, -Thr- or -Nva-; and
- (c) U is -(D)Ala-, -(D)Ser- or -[O-(2-hydroxyethyl)(D)Ser]-; or -[O-acyl(D)Ser]- or -[O-(2-acyloxyethyl)(D)Ser]-.

2. (Currently Amended) A cyclosporin analog according to Claim 1 or ~~a its~~ pro-drug or a pharmaceutically acceptable salt thereof, wherein in formula (I), B is -αAbu-, and U is -(D)Ala-.

3. (Currently Amended) A cyclosporin analog according to Claim 1 or ~~a its~~ pro-drug or a pharmaceutically acceptable salt thereof, wherein in formula I:

- (i) A is of the formula ~~A1 or A2, wherein:~~



wherein

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X is absent; and

Y is selected from a group consisting of:

- i. -C(O)-O-R1 where R1 is hydrogen, C1-C6 alkyl optionally substituted with halogen, heterocyclics, aryl, C1-C6 alkoxy or C1-C6 alkylthio, halogen substituted C1-C6 alkoxy, or halogen substituted C1-C6 alkylthio;
- ii. -C(O)-S-R1 where R1 is hydrogen, C1-C6 alkyl optionally substituted with halogen, heterocyclics, aryl, C1-C6 alkoxy or C1-C6 alkylthio, halogen substituted C1-C6 alkoxy, or halogen substituted C1-C6 alkylthio; and
- iii. C(O)-OCH₂-OC(O)R2 where R2 is C1-C6 alkyl optionally substituted with halogen, C1-C6 alkoxy, C1-C6 alkylthio, heterocyclics, or aryl;

(ii) B is - α Abu-; and

(iii) U is -(D)Ala-.

4. (Currently Amended) A cyclosporin analog according to claim 1 or a its pro-drug or a pharmaceutically acceptable salt ~~thereof~~, selected from the group consisting of:
 Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₃;
 Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOH;
 Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOEt;
 Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₂CH₂CH₃;
 Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₂Ph;
 Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₂F;

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Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCHF₂;

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCF₃;

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₂CF₃;

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₂Cl;

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₂OCH₃;

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOCH₂OCH₂CH₂O CH₃;

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -C(=O)SCH₂Ph;

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is -CH₂CH₂CH₂-; Y = -COOCH₃; and

Compound of Formula (I) wherein B = - α Abu-, U = -(D)Ala-, X is absent, Y = -COOFmoc.

5. (Original) A chemical process for preparing a cyclosporin analog of formula I as claimed in Claim 1, comprising:

a. reacting a compound of formula I, wherein A= -MeBmt- with:

i. an olefin of formula CH₂=CH-X-Y, wherein X and Y are as defined in Claim 1; and

ii. a catalyst;

in the presence of a lithium salt in an organic solvent; and

b. hydrogenating the product of step a in an organic solvent under hydrogen with a catalyst;

and optionally converting the product of said reaction into a pharmaceutically acceptable salt.

6. (Original) The chemical process as claimed in Claim 5, wherein the catalyst in step (a) (ii) is Grubb's ruthenium alkylidene, Nolan's catalyst, a benzylidene catalyst or a molybdenum catalyst.

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7. (Original) The chemical process as claimed in Claim 5, wherein step (b) is performed at room temperature.

8. (Original) The chemical process as claimed in Claim 7, wherein the catalyst in step (b) is Palladium on carbon.

9. (Original) A pharmaceutical composition, said composition comprising at least one cyclosporin analog of formula 1 as claimed in Claim 1, said cyclosporin analog being present alone or in combination with a pharmaceutically acceptable carrier or excipient.

10. (Original) A method for treating diseases characterized by airflow obstruction in a subject in need of treatment which comprises the step of administering to said subject a therapeutically effective amount of at least one cyclosporin analog of formula I as claimed in Claim 1.

11. (Original) The method of Claim 10, wherein said disease is asthma.

12. (Original) The method of Claim 10, wherein the step of administering the cyclosporin analog of formula I is done by topical administration.

13. (Previously Added) A method for providing anti-inflammatory or immunosuppressive therapy in a subject in need of treatment, the method comprising administering to said subject a therapeutically effective amount of at least one cyclosporin analog of formula I as in claim 1.

14. (Previously Added) The method of claim 13, wherein said administering is accomplished topically.